

Claimed are:

1. Use of a drug in the preparation of a medicament for the treatment or prevention of an ophthalmologic disorder, wherein the drug inhibits, antagonizes, or short-circuits the visual cycle at a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell.
2. The use set forth in claim 1, wherein the ophthalmologic disorder comprises a macular degeneration.
3. The use set forth in claim 1 or claim 2, wherein the ophthalmologic disorder comprises Stargardt's disease.
4. The use set forth in any preceding claim, wherein the ophthalmologic disorder comprises lipofuscin accumulation.
5. The use set forth in any preceding claim, wherein the drug increases the rate at which 11-*cis*-retinal is isomerized to all-*trans*-retinal.
6. The use set forth in any preceding claim, wherein the drug inhibits, antagonizes, or short-circuits the visual cycle in the retinal pigment epithelium.
7. The use set forth in any preceding claim, wherein the drug inhibits or antagonizes the visual cycle in the retinal pigment epithelium.
8. The use set forth in claim 7, wherein the drug inhibits at least one of lecithin retinol acyl transferase, isomerohydrolase, and 11-*cis*-retinol dehydrogenase, or inhibits binding to RPE65.
9. The use set forth in any preceding claim, wherein the drug short-circuits the visual cycle in the retinal pigment epithelium.
10. The use set forth in any one of claims 1-9, wherein the medicament is administered chronically.
11. The use set forth in any one of claims 1-9, wherein the medicament is administered once.
12. The use set forth in any one of claims 1-9, wherein the medicament is administered weekly.
13. The use set forth in any one of claims 1-9, wherein the medicament is administered twice weekly.
14. The use set forth in any one of claims 1-13, wherein a second drug different from the first drug is used in the preparation of the medicament.

15. The use set forth in claim 14, wherein the second drug inhibits, antagonizes, or short-circuits the visual cycle at a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell.
16. The use set forth in claim 14, wherein both the first drug and second drug inhibit or antagonize a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell.
17. The use set forth in any one of claims 14-16, wherein the first drug and the second drug inhibit or antagonize different molecules.
18. The use set forth in any one of claims 14-17, wherein the first drug and the second drug inhibit or antagonize different steps in the visual cycle.
19. The use set forth in claim 18, wherein the first drug and the second drug inhibit or antagonize sequential steps in the visual cycle.
20. The use set forth in any one of claims 14-17, wherein the first drug and the second drug inhibit or antagonize the same step in the visual cycle.
21. The use set forth in any one of claims 14-20, wherein the first drug inhibits RPE65.
22. The use set forth in claim 21, wherein the second drug inhibits lecithin:retinol acyl transferase, isomeroxydrolase, and/or 11-cis-retinol dehydrogenase.
23. The use set forth in any one of claims 14-21, wherein the first drug inhibits or antagonizes a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell, and the second drug short-circuits the visual cycle at a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell.
24. A method of treating or preventing an ophthalmologic disorder in a subject, the method comprising:  
administering to the subject a drug that inhibits, antagonizes, or short-circuits the visual cycle at a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell.
25. A method of treating or preventing macular degeneration, the method comprising:  
administering a drug to a subject in need of treating or preventing macular degeneration, wherein the drug inhibits, antagonizes, or short-circuits the visual cycle at a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell.
26. The method of any of claims 24-25, further comprising diagnosing macular degeneration in the subject.
27. The method of any of claims 24-26, further comprising monitoring the macular degeneration in the subject.

28. The method of any of claims 24-27, wherein the ophthalmologic disorder comprises a macular degeneration.
29. The method of any of claims 24-28, wherein the ophthalmologic disorder comprises Stargardt's disease.
30. The method of any of claims 24-29, wherein the ophthalmologic disorder comprises lipofuscin accumulation.
31. The method of any of claims 24-30, wherein the drug increases the rate at which 11-*cis*-retinal is isomerized to all-*trans*-retinal.
32. The method of any of claims 24-31, wherein the drug inhibits, antagonizes, or short-circuits the visual cycle in the retinal pigment epithelium.
33. The method of any of claims 24-32, wherein the drug inhibits or antagonizes the visual cycle in the retinal pigment epithelium.
34. The use set forth claim 33, wherein the drug inhibits at least one of lecithin retinol acyl transferase, isomerohydrolase, and 11-*cis*-retinol dehydrogenase, or inhibits binding to RPE65.
35. The method of any of claims 24-34, wherein the drug short-circuits the visual cycle in the retinal pigment epithelium.
36. The method of any of claims 24-35, wherein the medicament is administered chronically.
37. The method of any of claims 24-35, wherein the medicament is administered once.
38. The method of any of claims 24-35, wherein the medicament is administered weekly.
39. The method of any of claims 24-35, wherein the medicament is administered twice weekly.
40. The method of any of claims 24-39, wherein a second drug different from the first drug is used in the preparation of the medicament.
41. The method of claim 40, wherein the second drug inhibits, antagonizes, or short-circuits the visual cycle at a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell.
42. The method of claim 40, wherein both the first drug and second drug inhibit or antagonize a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell.
43. The method of claim 41 or 42, wherein the first drug and the second drug inhibit or antagonize different molecules.

44. The method of any one of claims 40-43, wherein the first drug and the second drug inhibit or antagonize different steps in the visual cycle.

45. The method of claim 44, wherein the first drug and the second drug inhibit or antagonize sequential steps in the visual cycle.

46. The method of any one of claims 40-43, wherein the first drug and the second drug inhibit or antagonize the same step in the visual cycle.

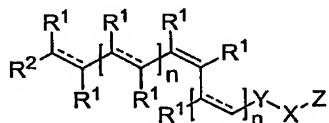
47. The method of any one of claims 40-46, wherein the first drug inhibits RPE65.

48. The method of claim 47, wherein the second drug inhibits lecithin retinol acyl transferase, isomerohydrolase, and/or 11-cis-retinol dehydrogenase.

49. The method of any one of claims 40-47, wherein the first drug inhibits or antagonizes a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell, and the second drug short-circuits the visual cycle at a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell.

50. A use as set forth in any one of claims 1-23 or a method as set forth in any one of claims 24-49, wherein the drug comprises a compound as defined by any one of claims 51-257.

51. A compound of formula I:

**I**

wherein, independently for each occurrence,

n is 0 to 10 inclusive;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, or aralkyl;

Y is -C(R<sub>b</sub>)<sub>p</sub>-, -C(=O)- or -C(R<sub>b</sub>)<sub>p</sub>C(=O)-;

X is -O-, -N(R<sub>a</sub>)-, -C(R<sub>b</sub>)<sub>p</sub>- or -S-;

Z is alkyl, haloalkyl, -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>p</sub>R<sub>b</sub> or -C(=O)R<sub>b</sub>;

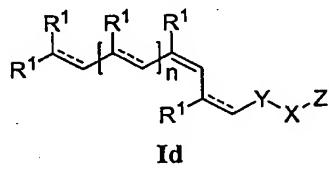
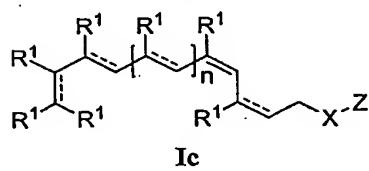
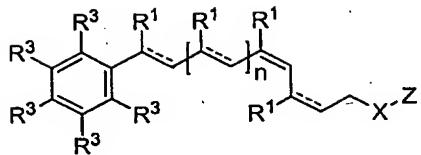
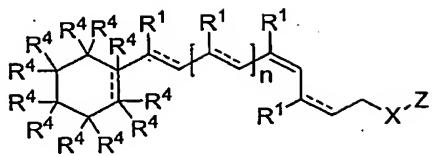
p is 0 to 20 inclusive;

R<sub>a</sub> is hydrogen, alkyl, aryl or aralkyl;

R<sub>b</sub> is hydrogen, alkyl or haloalkyl; and

— denotes a single bond, a *cis* double bond, or a *trans* double bond.

52. A compound of formula Ia, Ib, Ic or Id:



wherein, independently for each occurrence,

$n$  is 0 to 4 inclusive;

$R^1$  is hydrogen or alkyl;

$R^3$  is hydrogen, halogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroaralkyl, heteroaralkylenyl, heteroaralkynyl, cyano, nitro, sulphydryl, hydroxyl, sulfonyl, amino, acylamino, amido, alkylthio, carboxyl, carbamoyl, alkoxy, sulfonate, sulfate, sulfonamido, sulfamoyl, sulfonyl, and sulfoxido;

$R^4$  is absent, hydrogen, halogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, aralkylenyl, aralkynyl, heteroaralkyl, heteroaralkylenyl, heteroaralkynyl, cyano, nitro, sulphydryl, hydroxyl, sulfonyl, amino, acylamino, amido, alkylthio, carboxyl, carbamoyl, alkoxy, sulfonate, sulfate, sulfonamido, sulfamoyl, sulfonyl, and sulfoxido;

$Y$  is  $-C(R_b)_2-$  or  $-C(=O)-$ ;

$X$  is  $-O-$ ,  $-N(R_a)-$ ,  $-C(R_b)_2-$  or  $-S-$ ;

$Z$  is alkyl, haloalkyl or  $-C(=O)R_b$ ;

$R_a$  is hydrogen, alkyl, aryl or aralkyl;

$R_b$  is hydrogen, alkyl or haloalkyl; and

— denotes a single bond, a *cis* double bond, or a *trans* double bond.

53. The compound of claim 52, wherein  $R^1$  is methyl.
54. The compound of claim 52 or claim 53, wherein  $n$  is 0.
55. The compound of claim 52 or claim 53, wherein  $n$  is 1.
56. The compound of any one of claims 52-55, wherein  $Y$  is  $-CH_2-$ .
57. The compound of any one of claims 52-56, wherein  $X$  is  $-O-$ .
58. The compound of any one of claims 52-56, wherein  $X$  is  $-N(H)-$ .
59. The compound of any one of claims 52-58, wherein  $Z$  is  $-C(=O)R_b$ .

60. The compound of any one of claims 52-58, wherein Z is  $-C(=O)R_b$ ; and  $R_b$  is haloalkyl.

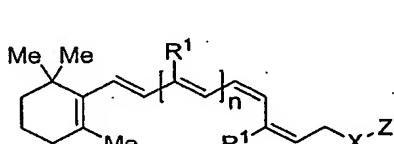
61. The compound of any one of claims 52-58, wherein Z is alkyl.

62. The compound of any one of claims 52-58, wherein Z is haloalkyl.

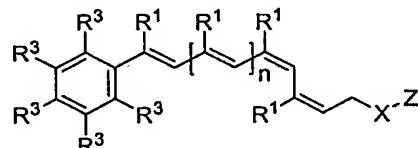
63. The compound of any one of claims 52-62, wherein  $R^3$  is hydrogen.

64. The compound of any one of claims 52-63, wherein  $R^4$  is hydrogen, methyl or absent.

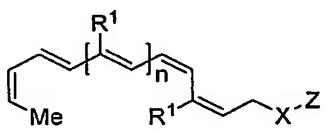
65. A compound of formula Ie, If, Ig, or Ih:



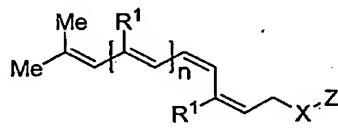
Ie



If



Ig



Ih

wherein, independently for each occurrence,

n is 0 to 4 inclusive;

$R^1$  is hydrogen or alkyl;

$R^3$  is hydrogen, halogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, aralkyenyl, aralkynyl, heteroaralkyl, heteroaralkyenyl, heteroaralkynyl, cyano, nitro, sulfhydryl, hydroxyl, sulfonyl, amino, acylamino, amido, alkylthio, carboxyl, carbamoyl, alkoxy, sulfonate, sulfate, sulfonamido, sulfamoyl, sulfonyl, and sulfoxido;

X is  $-O-$ ,  $-N(R_a)-$ ,  $-C(R_b)_2-$  or  $-S-$ ;

Z is alkyl, haloalkyl or  $-C(=O)R_b$ ;

$R_a$  is hydrogen, alkyl, aryl or aralkyl; and

$R_b$  is hydrogen, alkyl or haloalkyl.

66. The compound of claim 65, wherein n is 0.

67. The compound of claim 65, wherein n is 1.

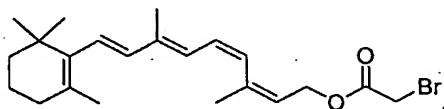
68. The compound of any one of claims 65-67, wherein X is  $-O-$ .

69. The compound of any one of claims 65-67, wherein X is  $-N(H)-$ .

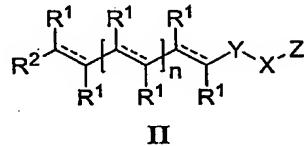
70. The compound of any one of claims 65-69, wherein Z is  $-C(=O)R_b$ .

71. The compound of any one of claims 65-69, wherein Z is  $-C(=O)R_b$ ; and  $R_b$  is haloalkyl.

72. The compound of any one of claims 65-69, wherein Z is alkyl.
73. The compound of any one of claims 65-69, wherein Z is haloalkyl.
74. The compound of any one of claims 65-73, wherein R<sup>3</sup> is hydrogen.
75. The compound of any one of claims 65-67 or claim 74, wherein X is -O-; and Z is alkyl.
76. The compound of any one of claims 65-67 or claim 74, wherein X is -O-; and Z is haloalkyl.
77. The compound of any one of claims 65-67 or claim 74, wherein X is -N(H)-; and Z is alkyl.
78. The compound of any one of claims 65-67 or claim 74, wherein X is -N(H)-; and Z is haloalkyl.



79. A compound having a structure represented by  
 80. A compound of formula II:



wherein

n is 0 to 10 inclusive;

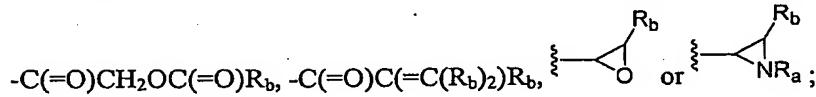
R<sup>1</sup> is hydrogen or alkyl;

$R^2$  is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, or aralkyl;

Y is  $-C(R_b)_p-$ ,  $-C(=O)-$  or  $-C(R_b)_pC(=O)-$ ;

X is hydrogen, -O-, -S-, -N(R<sub>a</sub>)-, -N(R<sub>a</sub>)-N(R<sub>a</sub>)-, -C(=O)-, -C(=NR<sub>a</sub>)-, -C(=NOH)-, -C(=S)- or -C(R<sub>b</sub>)<sub>p</sub>-;

Z is absent, hydrogen, alkyl, haloalkyl, aryl, aralkyl, -CN, -OR<sub>b</sub>, -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>p</sub>R<sub>b</sub>, -C(=O)R<sub>b</sub>, -C(=O)CH<sub>2</sub>F, -C(=O)CHF<sub>2</sub>, -C(=O)CF<sub>3</sub>, -C(=O)CHN<sub>2</sub>, -C(=O)OR<sub>b</sub>,



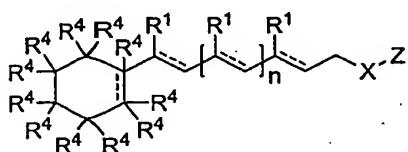
p is 0 to 20 inclusive;

$R_a$  is hydrogen, alkyl, aryl or aralkyl;

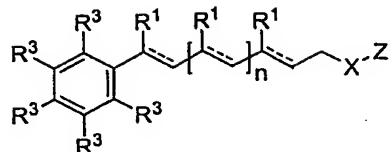
$R_b$  is hydrogen, alkyl, haloalkyl, aryl or aralkyl; and

$\text{---}$  denotes a single bond, a *cis* double bond or a *trans* double bond.

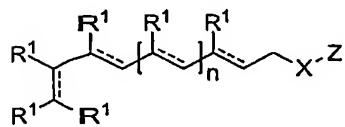
## 81. A compound of formula IIa, IIb, IIc, or IId:



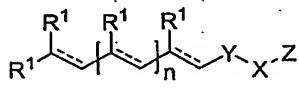
IIa



IIb



IIc



IId

wherein, independently for each occurrence,

n is 0 to 4 inclusive;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>3</sup> is hydrogen, halogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, aralkyenyl, aralkynyl, heteroaralkyl, heteroaralkyenyl, heteroaralkynyl, cyano, nitro, sulphydryl, hydroxyl, sulfonyl, amino, acylamino, amido, alkylthio, carboxyl, carbamoyl, alkoxy, sulfonate, sulfate, sulfonamido, sulfamoyl, sulfonyl, and sulfoxido;

R<sup>4</sup> is absent, hydrogen, halogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, aralkyenyl, aralkynyl, heteroaralkyl, heteroaralkyenyl, heteroaralkynyl, cyano, nitro, sulphydryl, hydroxyl, sulfonyl, amino, acylamino, amido, alkylthio, carboxyl, carbamoyl, alkoxy, sulfonate, sulfate, sulfonamido, sulfamoyl, sulfonyl, and sulfoxido;

Y is -C(=O)- or -C(R<sub>b</sub>)<sub>2</sub>-;

X is hydrogen, -O-, -S-, -N(R<sub>a</sub>)-, -N(R<sub>a</sub>)-N(R<sub>a</sub>)-, -C(=O)-, -C(=NR<sub>a</sub>)-, -C(=NOH)-, -C(=S)- or -C(R<sub>b</sub>)<sub>2</sub>-;

Z is absent, hydrogen, alkyl, haloalkyl, aryl, aralkyl, -CN, -OR<sub>b</sub>, -C(=O)R<sub>b</sub>, -C(=O)CH<sub>2</sub>F, -C(=O)CHF<sub>2</sub>, -C(=O)CF<sub>3</sub>, -C(=O)CHN<sub>2</sub>, -C(=O)CH<sub>2</sub>OC(=O)R<sub>b</sub>,

-C(=O)OR<sub>b</sub>, -C(=O)C(=C(R<sub>b</sub>)<sub>2</sub>)R<sub>b</sub>, or

R<sub>a</sub> is hydrogen, alkyl, aryl or aralkyl;

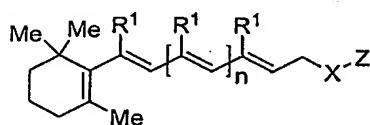
R<sub>b</sub> is hydrogen, alkyl, haloalkyl, aryl or aralkyl; and

— denotes a single bond, a cis double bond or a trans double bond.

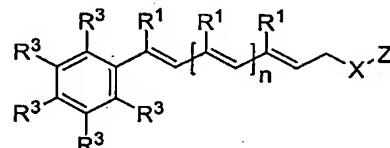
82. The compound of claim 81, wherein n is 0.

83. The compound of claim 81, wherein n is 1.

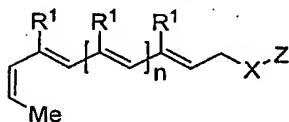
84. The compound of any one of claims 81-83, wherein R<sup>1</sup> is hydrogen or methyl.
85. The compound of any one of claims 81-84, wherein R<sup>3</sup> is hydrogen.
86. The compound of any one of claims 81-85, wherein R<sup>4</sup> is hydrogen or methyl.
87. The compound of any one of claims 81-86, wherein Y is -CH<sub>2</sub>-.
88. The compound of any one of claims 81-87, wherein X is -O-.
89. The compound of any one of claims 81-87, wherein X is -NH-.
90. The compound of any one of claims 81-87, wherein X is -C(R<sub>b</sub>)<sub>2</sub>-.
91. The compound of any one of claims 81-87, wherein X is -C(=O)-.
92. The compound of any one of claims 81-91, wherein Z is alkyl.
93. The compound of any one of claims 81-91, wherein Z is haloalkyl.
94. A compound of formula IIe, IIIf, IIg, or IIIh:



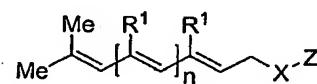
IIe



IIIf



IIg



IIIh

wherein, independently for each occurrence,

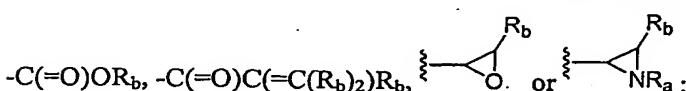
n is 0 to 4 inclusive;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>3</sup> is hydrogen, halogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, aralkylenyl, aralkynyl, heteroaralkyl, heteroaralkylenyl, heteroaralkynyl, cyano, nitro, sulphydryl, hydroxyl, sulfonyl, amino, acylamino, amido, alkylthio, carboxyl, carbamoyl, alkoxy, sulfonate, sulfate, sulfonamido, sulfamoyl, sulfonyl, and sulfoxido;

X is hydrogen, -O-, -S-, -N(R<sub>a</sub>)-, -N(R<sub>a</sub>)-N(R<sub>a</sub>)-, -C(=O)-, -C(=NR<sub>a</sub>)-, -C(=NOH)-, -C(=S)- or -C(R<sub>b</sub>)<sub>2</sub>-;

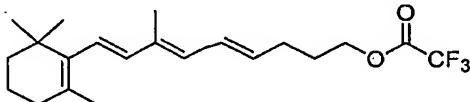
Z is absent, hydrogen, alkyl, haloalkyl, aryl, aralkyl, -CN, -OR<sub>b</sub>, -C(=O)R<sub>b</sub>, -C(=O)CH<sub>2</sub>F, -C(=O)CHF<sub>2</sub>, -C(=O)CF<sub>3</sub>, -C(=O)CHN<sub>2</sub>, -C(=O)CH<sub>2</sub>OC(=O)R<sub>b</sub>,



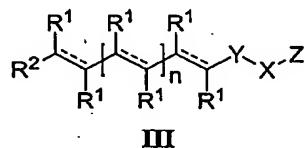
R<sub>a</sub> is hydrogen, alkyl, aryl or aralkyl; and

R<sub>b</sub> is hydrogen, alkyl, haloalkyl, aryl or aralkyl.

- 95. The compound of claim 94, wherein n is 0.
- 96. The compound of claim 94, wherein n is 1.
- 97. The compound of any one of claims 94-96, wherein R<sup>1</sup> is hydrogen or methyl.
- 98. The compound of any one of claims 94-97, wherein R<sup>3</sup> is hydrogen.
- 99. The compound of any one of claims 94-98, wherein R<sup>4</sup> is hydrogen or methyl.
- 100. The compound of any one of claims 94-99, wherein X is -O-.
- 101. The compound of any one of claims 94-99, wherein X is -NH-.
- 102. The compound of any one of claims 94-99, wherein X is -CH<sub>2</sub>-.
- 103. The compound of any one of claims 94-99, wherein X is -C(=O)-.
- 104. The compound of any one of claims 94-103, wherein Z is alkyl.
- 105. The compound of any one of claims 94-103, wherein Z is haloalkyl.
- 106. The compound of any one of claims 94-103, wherein Z is -C(=O)R<sub>b</sub>.
- 107. The compound of any one of claims 94-98, wherein X is -O-; and Z is -C(=O)R<sub>b</sub>.
- 108. The compound of any one of claims 94-98, wherein X is -CH<sub>2</sub>-; and Z is -C(=O)R<sub>b</sub>.
- 109. The compound of any one of claims 94-98, wherein X is -NH-; and Z is -C(=O)R<sub>b</sub>.
- 110. A compound having a structure represented by



- 111. A compound of formula III:



wherein

n is 0 to 10 inclusive;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, or aralkyl;

Y is -CR<sub>b</sub>(OR<sub>b</sub>)-, -CR<sub>b</sub>(N(R<sub>a</sub>)<sub>2</sub>)-, -C(R<sub>b</sub>)<sub>p</sub>, -C(=O)- or -C(R<sub>b</sub>)<sub>p</sub>C(=O)-;

X is -O-, -S-, -N(R<sub>a</sub>)-, -C(=O)-, or -C(R<sub>b</sub>)<sub>p</sub>-;

Z is hydrogen, alkyl, haloalkyl, aryl, aralkyl, -OR<sub>b</sub>, -N(R<sub>b</sub>)<sub>2</sub>, -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>p</sub>R<sub>b</sub>,

-C(=O)R<sub>b</sub>, -C(=NIR<sub>a</sub>)R<sub>b</sub>, -C(=NOR<sub>b</sub>)R<sub>b</sub>, -C(OR<sub>b</sub>)(R<sub>b</sub>)<sub>2</sub>, -C(N(R<sub>a</sub>)<sub>2</sub>)(R<sub>b</sub>)<sub>2</sub> or

-(CH<sub>2</sub>CH<sub>2</sub>O)<sub>p</sub>R<sub>b</sub>;

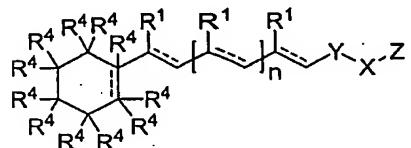
p is 0 to 20 inclusive;

R<sub>a</sub> is hydrogen, alkyl, aryl or aralkyl;

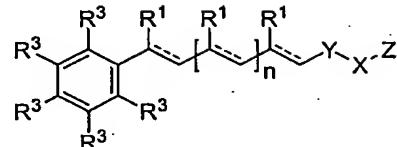
R<sub>b</sub> is hydrogen, alkyl, haloalkyl, aryl or aralkyl; and

— denotes a single bond or a *trans* double bond.

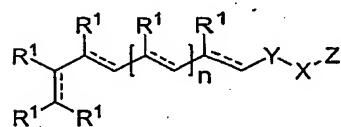
112. A compound of formula IIIa, IIIb, IIIc or IIId:



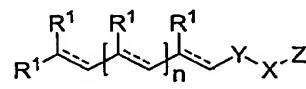
IIIa



IIIb



IIIc



IIId

wherein, independently for each occurrence,

n is 0 to 4 inclusive;

R<sup>1</sup> is hydrogen or alkyl;

Y is -C(=O)-, -CR<sub>b</sub>(OR<sub>b</sub>)-, -CR<sub>b</sub>(N(R<sub>a</sub>)<sub>2</sub>)- or -C(R<sub>b</sub>)<sub>2</sub>-;

X is -O-, -S-, -N(R<sub>a</sub>)-, -C(=O)-, or -C(R<sub>b</sub>)<sub>2</sub>-;

Z is hydrogen, alkyl, haloalkyl, aryl, aralkyl, -OR<sub>b</sub>, -N(R<sub>b</sub>)<sub>2</sub>, -C(=O)R<sub>b</sub>, -C(=NR<sub>a</sub>)R<sub>b</sub>, -C(=NOH)R<sub>b</sub>, -C(OR<sub>b</sub>)(R<sub>b</sub>)<sub>2</sub>, -C(N(R<sub>a</sub>)<sub>2</sub>)(R<sub>b</sub>)<sub>2</sub> or -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>p</sub>R<sub>b</sub>;

R<sub>a</sub> is hydrogen, alkyl, aryl or aralkyl;

R<sub>b</sub> is hydrogen, alkyl, haloalkyl, aryl or aralkyl;

p is 0 to 10 inclusive; and

— denotes a single bond or a *trans* double bond.

113. The compound of claim 112, wherein n is 0.

114. The compound of claim 112, wherein n is 1.

115. The compound of any one of claims 112-114, wherein R<sup>1</sup> is hydrogen or methyl.

116. The compound of any one of claims 112-115, wherein R<sup>3</sup> is hydrogen.

117. The compound of any one of claims 112-116, wherein R<sup>4</sup> is hydrogen or methyl.

118. The compound of any one of claims 112-117, wherein X is -O-.

119. The compound of any one of claims 112-117, wherein X is -NH-.

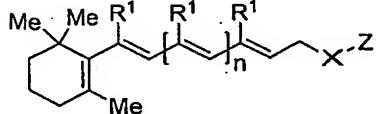
120. The compound of any one of claims 112-117, wherein X is -C(R<sub>b</sub>)<sub>2</sub>-.

121. The compound of any one of claims 112-117, wherein X is -C(=O)-.

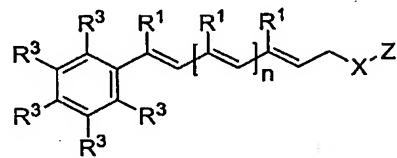
122. The compound of any one of claims 112-121, wherein Z is alkyl.

123. The compound of any one of claims 112-121, wherein Z is haloalkyl.

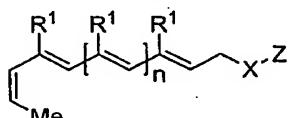
124. A compound of formula IIIe, IIIf, IIIg, or IIIh:



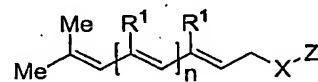
IIIe



IIIf



IIIg



IIIh

wherein, independently for each occurrence,

n is 0 to 4 inclusive;

R<sup>1</sup> is hydrogen or alkyl;

X is -O-, -S-, -N(R<sub>a</sub>)-, -C(=O)-, or -C(R<sub>b</sub>)<sub>2</sub>-;

Z is hydrogen, alkyl, haloalkyl, aryl, aralkyl, -OR<sub>b</sub>, -N(R<sub>b</sub>)<sub>2</sub>, -C(=O)R<sub>b</sub>, -C(=NR<sub>a</sub>)R<sub>b</sub>, -C(=NOH)R<sub>b</sub>, -C(OR<sub>b</sub>)(R<sub>b</sub>)<sub>2</sub>, -C(N(R<sub>a</sub>)<sub>2</sub>)(R<sub>b</sub>)<sub>2</sub> or -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>p</sub>R<sub>b</sub>;

R<sub>a</sub> is hydrogen, alkyl, aryl or aralkyl;

R<sub>b</sub> is hydrogen, alkyl, haloalkyl, aryl or aralkyl; and

p is 0 to 10 inclusive.

125. The compound of claim 124, wherein n is 0.

126. The compound of claim 124, wherein n is 1.

127. The compound of any one of claims 124-126, wherein R<sup>1</sup> is hydrogen or methyl.

128. The compound of any one of claims 124-127, wherein Y is -C(=O)-.

129. The compound of any one of claims 124-127, wherein Y is -CH<sub>2</sub>-.

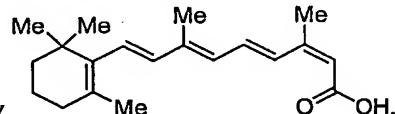
130. The compound of any one of claims 124-129, wherein Z is -C(=O)R<sub>b</sub>.

131. The compound of any one of claims 124-129, wherein Z is -CH(OH)R<sub>b</sub>-.

132. The compound of any one of claims 124-129, wherein Z is -CH(NH)R<sub>b</sub>.

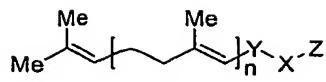
133. The compound of any one of claims 124-129, wherein Z is alkyl.

134. The compound of any one of claims 124-129, wherein Z is haloalkyl.



135. A compound having a structure represented by

## 136. A compound of formula IV:



wherein, independently for each occurrence,

n is 1, 2, 3 or 4;

Y is -C(R<sub>b</sub>)<sub>2</sub>- or -C(=O)-;

X is -O-, -NR<sub>a</sub>-, -C(R<sub>b</sub>)<sub>2</sub>- or -C(=O)-;

Z is -C(=O)R<sub>b</sub>, -OR<sub>b</sub>, -N(R<sub>b</sub>)<sub>2</sub>, alkyl or haloalkyl;

R<sub>a</sub> is hydrogen, alkyl, haloalkyl, aryl or aralkyl; and

R<sub>b</sub> is hydrogen, alkyl, haloalkyl, aryl or aralkyl.

137. The compound of claim 136, wherein Y is -CH<sub>2</sub>-.

138. The compound of claim 136 or claim 137, wherein X is -O-.

139. The compound of any one of claims 136-138, wherein Z is -C(=O)R<sub>b</sub>; and R<sub>b</sub> is alkyl.

140. The compound of any one of claims 136-138, wherein Z is alkyl.

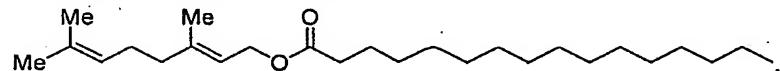
141. The compound of claim 136, wherein Y is -CH<sub>2</sub>-; X is -O-; Z is -C(=O)R<sub>b</sub>; and R<sub>b</sub> is alkyl.

142. The compound of claim 136, wherein Y is -CH<sub>2</sub>-; X is -O-; and Z is alkyl.

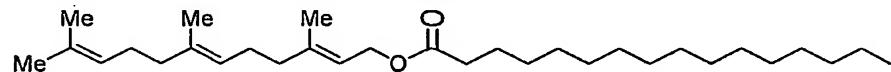
143. The compound of claim 136, wherein Y is -CH<sub>2</sub>-; X is -C(=O)-; and Z is alkyl.

144. The compound of claim 136, wherein Y is -CH<sub>2</sub>-; X is -C(=O)-; Z is -N(R<sub>b</sub>)<sub>2</sub>; and R<sub>b</sub> is alkyl.

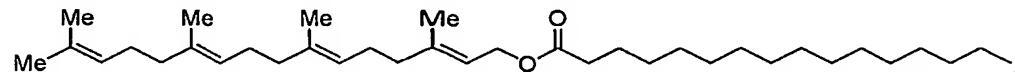
145. A compound having a structure represented by



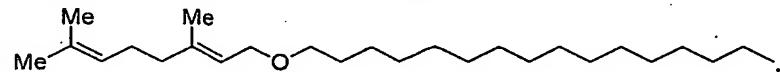
146. A compound having a structure represented by



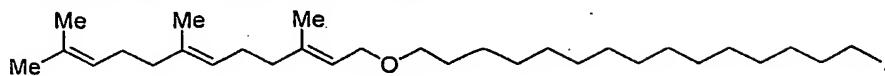
147. A compound having a structure represented by



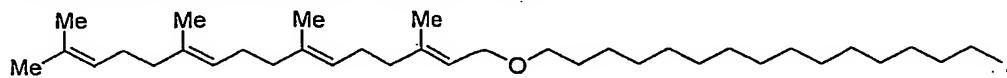
148. A compound having a structure represented by



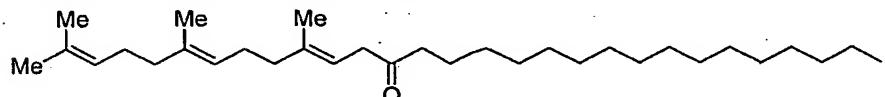
149. A compound having a structure represented by



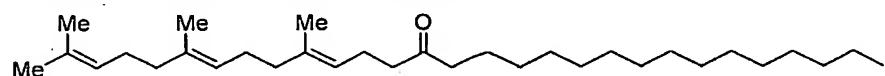
150. A compound having a structure represented by



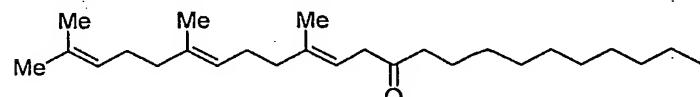
151. A compound having a structure represented by



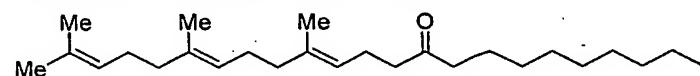
152. A compound having a structure represented by



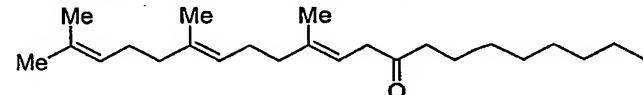
153. A compound having a structure represented by



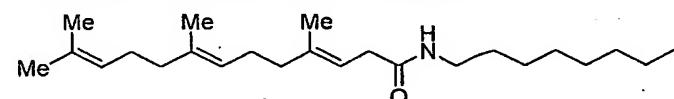
154. A compound having a structure represented by



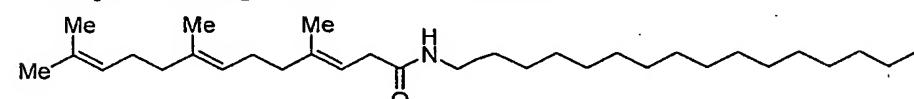
155. A compound having a structure represented by



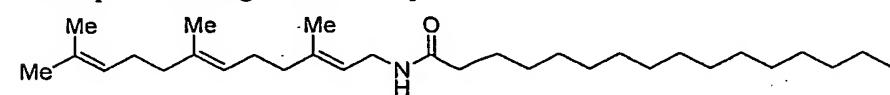
156. A compound having a structure represented by



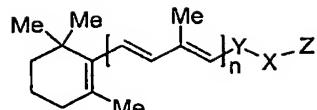
157. A compound having a structure represented by



158. A compound having a structure represented by



159. A compound of formula V:



wherein, independently for each occurrence,

n is 1, 2 or 3;

Y is  $-C(R_b)_2-$ ,  $-C(=O)-$  or  $-CH(OH)-$ ;

X is  $-O-$ ,  $-NR_a-$  or  $-C(R_b)_2-$ ;

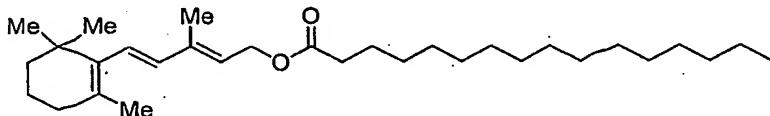
Z is  $-C(=O)R_b$ , hydrogen,  $-(CH_2CH_2O)_pR_b$ , alkyl or haloalkyl;

$R_a$  is hydrogen, alkyl, haloalkyl, aryl or aralkyl;

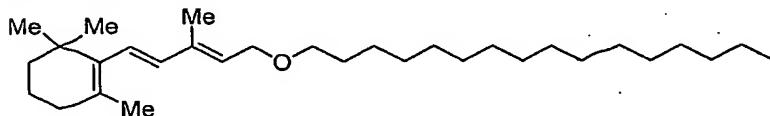
$R_b$  is hydrogen, alkyl, haloalkyl, aryl or aralkyl; and

p is 1 to 10 inclusive.

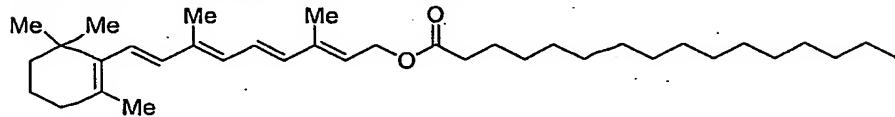
160. The compound of claim 159, wherein Y is  $-CH_2-$ .
161. The compound of claim 159, wherein Y is  $-C(=O)-$ .
162. The compound of claim 159, wherein Y is  $-CH(OH)-$ .
163. The compound of any one of claims 159-162, wherein X is  $-O-$ .
164. The compound of any one of claims 159-162, wherein X is  $-NR_a-$ .
165. The compound of any one of claims 159-162, wherein X is  $-C(R_b)-$ .
166. The compound of any one of claims 159-165, wherein Z is alkyl.
167. The compound of any one of claims 159-165, wherein Z is  $-C(=O)R_b$ ; and  $R_b$  is alkyl.
168. The compound of any one of claims 159-165, wherein Z is  $-(CH_2CH_2O)_pR_b$ ; and  $R_b$  is alkyl.
169. A compound having a structure represented by



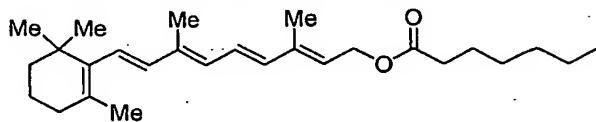
170. A compound having a structure represented by



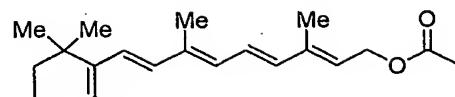
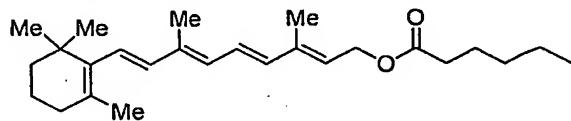
171. A compound having a structure represented by



172. A compound having a structure represented by



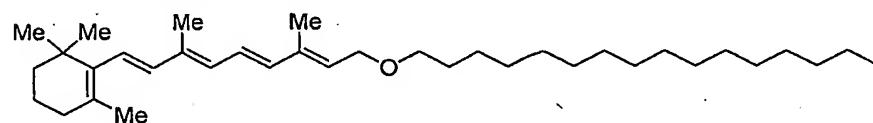
173. A compound having a structure represented by



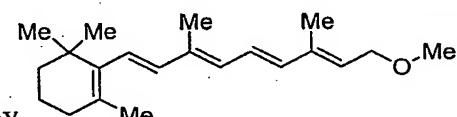
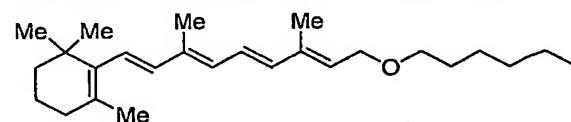
174. A compound having a structure represented by



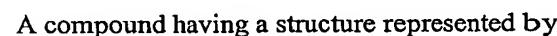
175. A compound having a structure represented by



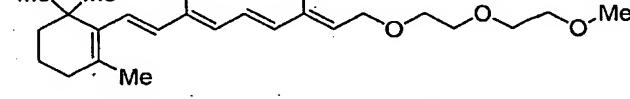
176. A compound having a structure represented by



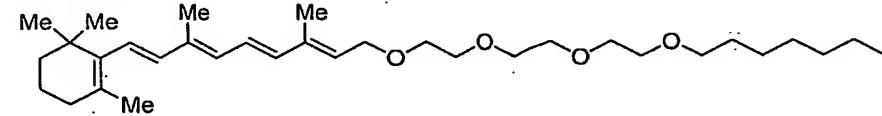
177. A compound having a structure represented by



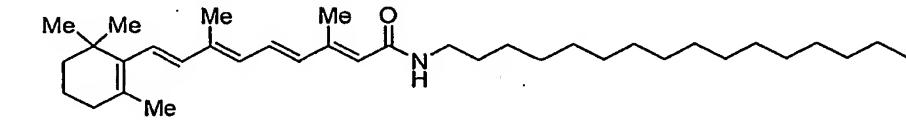
178. A compound having a structure represented by

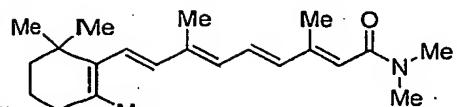


179. A compound having a structure represented by



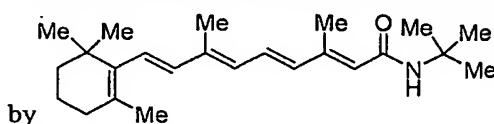
180. A compound having a structure represented by



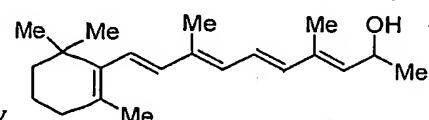
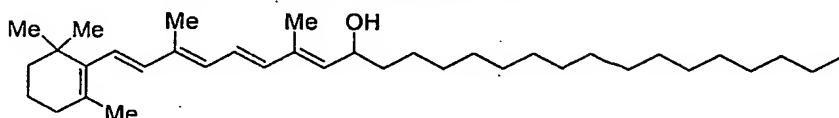


181. A compound having a structure represented by

182. A compound having a structure represented

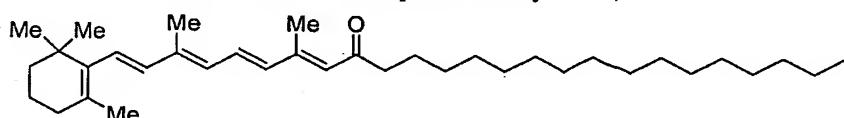


183. A compound having a structure represented by

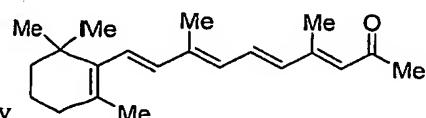
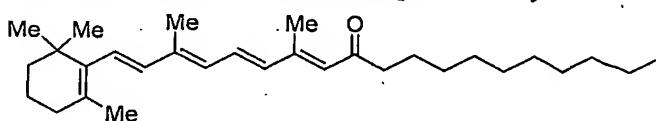


184. A compound having a structure represented by

185. A compound having a structure represented by

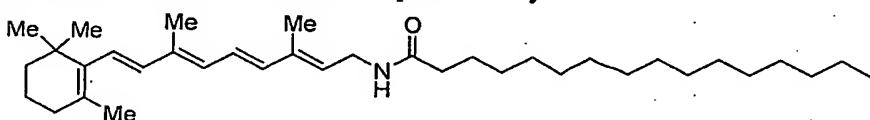


186. A compound having a structure represented by

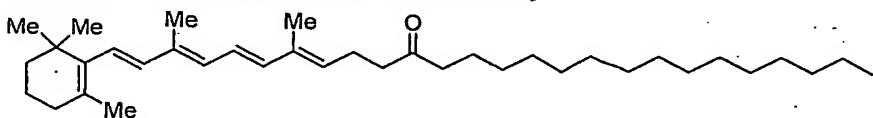


187. A compound having a structure represented by

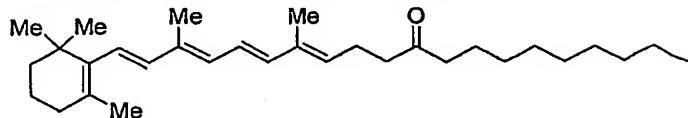
188. A compound having a structure represented by



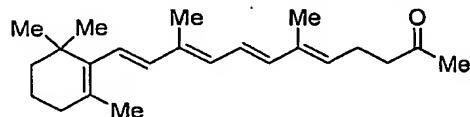
189. A compound having a structure represented by



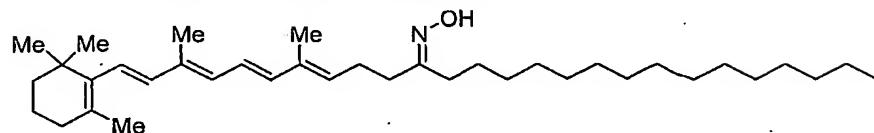
190. A compound having a structure represented by



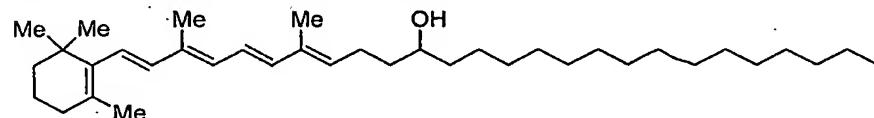
191. A compound having a structure represented by



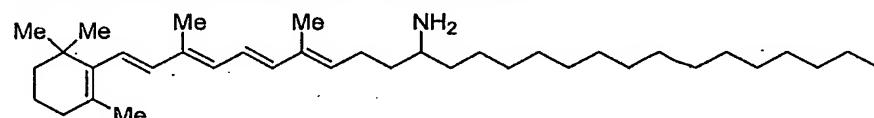
192. A compound having a structure represented by



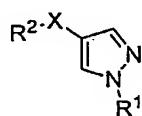
193. A compound having a structure represented by



194. A compound having a structure represented by



195. A compound of formula VI:



VI

wherein, independently for each occurrence,

R<sup>1</sup> is hydrogen, alkyl, aryl or aralkyl;

X is alkyl, alkenyl, -C(R<sub>b</sub>)<sub>2</sub>- or -C(=O)-;

R<sup>2</sup> is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, or aralkyl;

R<sub>a</sub> is hydrogen, alkyl, aryl or aralkyl; and

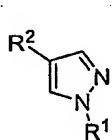
R<sub>b</sub> is hydrogen or alkyl.

196. The compound of claim 195, wherein R<sup>1</sup> is hydrogen.

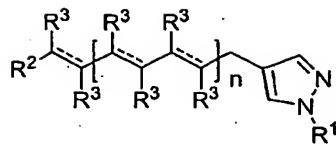
197. The compound of claim 195 or claim 196, wherein X is -C(R<sub>b</sub>)<sub>2</sub>-.

198. The compound of claim 195 or claim 196, wherein X is -C(=O)-.

199. A compound of formula VIa or VIb:



VIa



VIb

wherein, independently for each occurrence,

R<sup>1</sup> is hydrogen, alkyl, aryl or aralkyl;

R<sup>2</sup> is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, or aralkyl;

R<sup>3</sup> is hydrogen or alkyl;

R<sub>a</sub> is hydrogen, alkyl, aryl or aralkyl;

R<sub>b</sub> is hydrogen or alkyl; and

— denotes a single bond, a *cis* double bond, or a *trans* double bond.

200. The compound of claim 199, wherein R<sup>1</sup> is hydrogen.

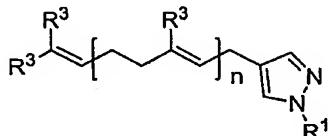
201. The compound of claim 199 or claim 200, wherein R<sup>2</sup> is alkyl.

202. The compound of any one of claims 199-201, wherein R<sup>3</sup> is hydrogen or methyl.

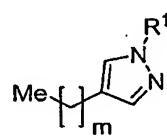
203. A compound of formula VIc, VIId or VIe:



VIc



VIId



VIe

wherein, independently for each occurrence,

n is 1 to 5 inclusive;

m is 0 to 30 inclusive;

R<sup>1</sup> is hydrogen, alkyl, aryl or aralkyl;

R<sup>2</sup> is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, or aralkyl;

R<sup>3</sup> is hydrogen or alkyl;

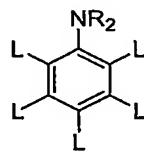
R<sup>4</sup> is hydrogen, halogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, aralkylenyl, aralkynyl, heteroaralkyl, heteroaralkylenyl, heteroaralkynyl, cyano, nitro, sulfhydryl, hydroxyl, sulfonyl, amino, acylamino, amido, alkylthio, carboxyl, carbamoyl, alkoxy, sulfonate, sulfate, sulfonamido, sulfamoyl, sulfonyl, and sulfoxido;

R<sub>a</sub> is hydrogen, alkyl, aryl or aralkyl; and

R<sub>b</sub> is hydrogen or alkyl.

204. The compound of claim 203, wherein R<sup>1</sup> is hydrogen.

- 205. The compound of claim 203, wherein R<sup>4</sup> is hydrogen.
- 206. The compound of claim 203, wherein R<sup>1</sup> is hydrogen; and R<sup>4</sup> is hydrogen.
- 207. The compound of any one of claims 203-206, wherein n is 1, 2 or 3.
- 208. The compound of any one of claims 203-207, wherein R<sup>3</sup> is methyl.
- 209. The compound of any one of claims 203 or 207-208, wherein R<sup>1</sup> is hydrogen.
- 210. The compound of any one of claims 203-206, wherein n is 1, 2 or 3; and R<sup>3</sup> is methyl.
- 211. The compound of claim 203, wherein n is 1, 2 or 3; R<sup>3</sup> is methyl; and R<sup>1</sup> is hydrogen.
- 212. The compound of any one of claims 203-211, wherein m is 1 to 10 inclusive.
- 213. The compound of any one of claims 203-211, wherein m is 11 to 20 inclusive.
- 214. The compound of claim 203, wherein m is 11 to 20 inclusive; and R<sup>1</sup> is hydrogen.
- 215. A compound of formula VII:



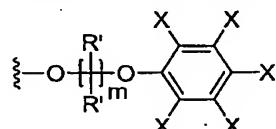
VII

wherein, independently for each occurrence:

R is H, alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl, or carbonyl;

L is a hydrophobic moiety, or any two adjacent L taken together form a fused aromatic or heteroaromatic ring.

- 216. The compound of claim 215, wherein L is alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl, carbonyl, ether, or polycyclic.
- 217. The compound of claim 215, wherein L has the formula VIIa:

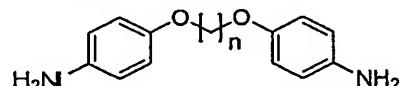


VIIa

wherein, independently for each occurrence:

R' and X are hydrogen, alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl, carbonyl, alkoxy, hydroxy, thiol, thioalkyl, or amino; and m is an integer from 1 to 6 inclusive.

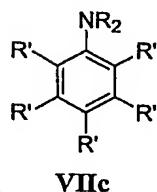
- 218. A compound of formula VIIb:



**VIIb**

wherein n is an integer from 1 to 8 inclusive.

219. A compound of formula VIIc:

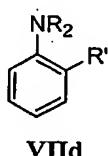


wherein, independently for each occurrence,

R is H, alkyl, or acyl; and

R' is alkyl or ether.

220. The compound of claim 219, wherein R is H for both occurrences.  
 221. The compound of claim 219, wherein at least one R is alkyl.  
 222. The compound of claim 219, wherein at least one R is methyl.  
 223. A compound of formula VIId:

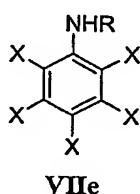


wherein, independently for each occurrence:

R is H, alkyl, or acyl; and

R' is alkyl or ether.

224. The compound of claim 223, wherein R is H for both occurrences.  
 225. The compound of claim 223, wherein at least one R is alkyl.  
 226. The compound of claim 223, wherein at least one R is methyl.  
 227. A compound of formula VIIe:



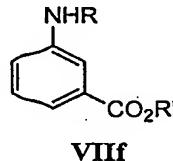
wherein, independently for each occurrence:

X is hydrogen or -C(=O)OR';

R is H, alkyl, or acyl; and

R' is alkyl.

- 228. The compound of claim 227, wherein R is H.
- 229. The compound of claim 227, wherein at least one R is alkyl.
- 230. The compound of claim 227, wherein R is methyl.
- 231. A compound of formula VIIf:



wherein, independently for each occurrence

- R is H, alkyl, or acyl; and
- R' is alkyl.

- 232. The compound of claim 231, wherein R is H.
- 233. The compound of claim 231, wherein at least one R is alkyl.
- 234. The compound of claim 231, wherein R is methyl.

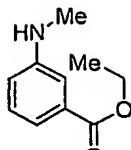
- 235. A compound having a structure represented by Nc1ccc(OCCOc2ccc(N)cc2)cc1.
- 236. A compound having a structure represented by Oc1ccc(NC(=O)C)c(O)cc1.

- 237. A compound having a structure represented by Nc1ccc(C(=O)OC)cc1.

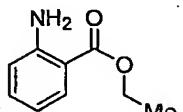
- 238. A compound having a structure represented by Nc1ccc(C2CCCC2)cc1.

- 239. A compound having a structure represented by Nc1ccc(C2CCCC2N)cc1.

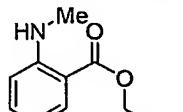
- 240. A compound having a structure represented by Nc1ccc2c(c1)COC(=O)C2.



241. A compound having a structure represented by

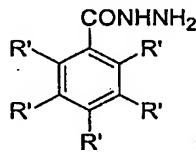


242. A compound having a structure represented by



243. A compound having a structure represented by

244. A compound of formula VIII:



VIII

wherein R' is hydrogen, alkyl or ether; or any two adjacent L taken together form a fused aromatic or heteroaromatic ring.

255. A compound of formula IX:



IX

wherein, independently for each occurrence:

R is H, alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl, or carbonyl; and

A is optionally substituted aryl or heteroaryl.

256. A compound of formula X:



X

wherein independently for each occurrence:

R' is hydrogen, alkyl or ether; and

A is optionally substituted aryl or heteroaryl.

257. A formulation comprising a compound defined by any one of claims 51-257 and a second compound, different from the first compound, also as defined by any one of claims 51-257.

258. A method of identifying a drug for treating or preventing an ophthalmologic disorder, comprising:  
administering a candidate drug to a subject having, or at risk for developing, the ophthalmologic disorder; and  
measuring accumulation of a retinotoxic compound in the retinal pigment epithelium (RPE) of the subject;  
wherein accumulation of the retinotoxic compound in the RPE in the presence of the candidate drug relative to the absence of the candidate drug indicates that the candidate drug is a drug for treating or preventing the ophthalmologic disorder.
259. A method of identifying a drug for treating or preventing an ophthalmologic disorder, comprising:  
contacting one or more cells representing an *in vitro* model of the visual cycle with the candidate drug; and  
measuring accumulation of a visual cycle intermediate product in at least one cell;  
wherein accumulation of the intermediate product in the presence of the candidate drug relative to the absence of the candidate drug indicates that the candidate drug is a drug for treating or preventing the ophthalmologic disorder.
260. The method of claim 259 or claim 259, wherein the ophthalmologic disorder comprises macular degeneration.
261. The method of any one of claims 259-260, wherein the ophthalmologic disorder comprises Stargardt's disease.
262. The method of any one of claims 259-161, wherein the ophthalmologic disorder comprises lipofuscin accumulation.
263. The method of any one of claims 259 or 261-262, wherein the retinotoxic compound is *N*-retinylidene-*N*-retinylethanolamine.
264. The method of any one of claims 260-262, wherein the intermediate is all-*trans*-retinal.